Another aspect, therefore, of the present invention provides a double mutant variant prothrombin or thrombin, WE, that has alanine substitutions both at the W215 and E217 positions. The amino acid sequence SEQ ID NO: 3 of the thrombin variant W215A/E217A is shown in Fig. 3, and that of the cleaved and enzymically active thrombin variant WE B-chain (SEQ ID NO: 4) is given in Fig. 4. As with the W215A variant thrombin (SEQ ID NO: 1), the amino acid substitution were introduced into an isolated nucleic acid encoding the thrombin protein by PCR-based mutagenesis, as described in Example 1, below. The sequence of the thrombin-encoding nucleic acid (SEQ ID NO: 5) ~~(GenBank Accession No._____)~~, having the W215A and E217A substitutions, is shown in Fig. 5. The sequence of the WE B-chain thrombin-encoding nucleic acid (SEQ ID NO: 12), having the W215A and E217A substitutions, is shown in Fig. 14. X-ray crystallgraphic data showing the orientation of the alanine substitutions in the double mutant W215A/E217A (WE) around the binding site of PPACK is shown in Fig. 6.

Please replace the paragraph at page 38, lines 20-23 with the following replacement paragraph:

In another embodiment of the variant thrombins of the present invention, the variant thrombin having the W215A and E217A substitutions is encoded by a nucleic acid comprising an amino acid sequence selected from SEQ ID NO: 5 and SEQ ID NO:6 ~~(GenBank Accession No._____)~~.

Please replace the paragraphs from page 56, lines 6-~~30~~ 18 to page 57, lines 1-11 with the following replacement paragraphs:

The antihemostatic effects of the antithrombotic enzymes were assessed following injection of 0.1, 0.2 or 0.45 mg/kg (1.8, 3.6 or 8 nmoles/kg) of APC or 0.011, 0.022, 0.055, 0.11 or 0.22 mg/kg (0.3, 0.6, 1.5, 3 or 6 nmoles/kg) of WE. Blood was drawn from the AV shunt, or by standard venepuncture in the high-dose WE studies when no thrombogenic shunt was inserted distal to the shunt. The total volume of blood drawn for all *in vitro* measurements was restricted to less than 10 mL per day in each study subject. Blood samples (0.45 or 0.9 mL) were drawn into 3.2% trisodium citrate at regular intervals for at least 100 mins. from time 0 (dosing) for immediate assessment of hemostasis by using point-of-care APTT testing. Samples were